Eosinophilic Meningitis Due to *Angiostrongylus cantonensis*

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VARIOUS HELMINTHIC INFECTIONS may cause eosinophilic meningitis, of which the most common in Australia and the South Pacific is the rat lungworm, *Angiostrongylus cantonensis*.[1] The diagnosis is usually suggested by clinical and epidemiologic features and confirmed with positive serologic tests.

The disease is an immediate complication of vegetarianism because humans usually become parasitized when they ingest vegetables contaminated by rat feces.

We describe four cases of this disease. All four patients are vegetarians. In the first patient, the disease was particularly severe, presumably reflecting a high parasite load. The other cases occurred in one family and illustrate how the severity of symptoms usually correlates with exposure to contaminated food.

Report of Cases

Patient 1

The patient, a 25-year-old male vegetarian who resided in Byron Bay, New South Wales, Australia, was seen because for two weeks he had had progressive lower limb weakness, dysesthesia of the feet, urinary incontinence, confusion, and visual hallucinations. Because of rapidly increasing weakness, he was transferred to the Royal Melbourne Hospital, Prahran, Victoria, Australia, in the fourth week of his illness. Before admission he had been living in an abandoned house infested with rats. His diet comprised home-grown vegetables that were rarely washed. He admitted to illicit drug use, including amphetamines, cocaine, and golden "magic" mushrooms.

On examination the patient was drowsy and disoriented and had a temperature of 37.5°C (99.5°F), moderate neck stiffness, and photophobia. Cranial nerves and fundi were normal. Motor power was globally decreased to 3/5 in all limbs, and areflexia and bilateral extensor plantar responses were noted. Sensation to pinprick was decreased below T-5. Anal tone was decreased, and an indwelling catheter was inserted for urinary retention.

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Cerebrospinal fluid (CSF) examination revealed the following: erythrocytes, 2×10^6 per liter; lymphocytes, 245×10^6 per liter; eosinophils, 75×10^6 per liter (22% of total leukocyte count); and monocytes, 19×10^6 per liter; the protein level was 1.01 grams per liter and glucose 1.9 mmol per liter. The CSF pressure was elevated at 33 cm of water. He had a peripheral blood leukocyte count of 21.2×10^9 per liter, of which 6.1×10^9 per liter (29% of total leukocyte count) was eosinophils (normal, 0.04 to 0.44) (Table 1). His erythrocyte sedimentation rate was 93 mm per hour (normal, 0 to 11). Liver function test results and a chest x-ray film were normal. Nerve conduction study findings were consistent with a multilevel radiculopathy. Electroencephalography showed generalized slowing of the background activity, consistent with an encephalopathy. A myelogram and cerebral computed tomographic (CT) scan were normal. Magnetic resonance imaging revealed a mild increase in ventricular size but no intraparenchymal lesion. Serologic tests for Epstein-Barr virus, human immunodeficiency virus, hepatitis B surface antigen, and CSF cryptococcal antigen were negative, as were cultures for *Cryptococcus* species and *Mycobacterium tuberculosis*. Serologic tests for *A cantonensis* (at another hospital) were initially negative at week 5 and became strongly positive at week 8.

Five weeks after his illness began, the patient's condition deteriorated, with fevers as high as 39°C (102.2°F) and complete lower limb paralysis. A spontaneous pneumothorax developed that required an intercostal catheter and was complicated by a bronchopleural fistula. Liver function test values became progressively abnormal with an alkaline phosphatase of 344 U per liter (normal, 0 to 90); bilirubin, 5 μmol per liter (normal, 0 to 19); aspartate aminotransferase, 331 U per liter (normal, 0 to 43); alanine aminotransferase, 363 U per liter (normal, 0 to 55); and γ-glutamyltransferase, 415 U per liter (normal, 0 to 50). A hepatic ultrasonogram was normal. Treatment with intravenous hydrocortisone sodium succinate, 100 mg every six hours, was started empirically; four days later this was changed to oral prednisolone, 75 mg daily. His clinical state improved. His confusional state resolved by week 7 of the illness, and there was a gradual return of upper and lower limb power. Fecal continence was regained, but recurrent urinary retention necessitated self-catheterization. Painful peripheral dysesthesias became a major problem as sensation returned. The peripheral blood eosinophilia resolved after steroid therapy was started, and there was resolution of the bronchopleural fistula. The liver function test values had returned to normal by week 13, and the erythrocyte sedimentation rate returned to normal by week 16. Steroid therapy was discontinued at week 17. The patient was discharged home six months after the onset of the illness, requiring the use of two canes for ambulation.

Patient 2

The patient, a 33-year-old woman, was admitted to the Austin Hospital, Heidelberg, because for three weeks she had had midthoracic back pain. This was associated

ABBREVIATIONS USED IN TEXT
CSF = cerebrospinal fluid
CT = computed tomographic

with hyperesthesia initially involving the left arm, then spreading to involve the whole body from the midthoracic region down.

Two weeks later, frontal headaches, photophobia, fevers, and diplopia developed. The patient was an Australian who had been residing in Vanuatu (formerly New Hebrides) for the past ten years. She returned to Australia for further medical care. Ironically, she was married to the manager of the local abattoir, but had recently commenced a vegetarian diet. She purchased salad vegetables from the markets in Port Vila, Vanuatu, which were not washed before consumption. She did not eat shellfish.

On examination, she had a temperature of 37.4°C (99.3°F). She had pronounced cutaneous hyperesthesia, being unable to tolerate the feel of clothing or bedsheets on her skin. She had photophobia and mild neck stiffness. There was a partial left sixth cranial nerve palsy. The fundi were normal. Further findings of the examination were unremarkable.

A CT scan of the brain was normal. A lumbar puncture was done, and the CSF pressure was elevated at 44 cm of water. The CSF glucose content was 2.7 mmol per liter, and the protein value was 0.37 grams per liter. The cell count showed lymphocytes, 160 × 10^6 per liter; eosinophils, 48 × 10^6 per liter (22% of total leukocyte count); neutrophils, 12 × 10^6 per liter; and erythrocytes, 5 × 10^6 per liter. The CSF cryptococcal antigen test and cultures for *Cryptococcus* species and *M tuberculosis* were negative.

Her peripheral leukocyte count was 12.2 × 10^9 per liter with eosinophilia (18%). Serum electrolyte tests showed a lowered sodium level of 116 mmol per liter. Serum and urine osmolalities confirmed a diagnosis of inappropriate antidiuretic hormone secretion. Liver function test results, a chest x-ray film, and x-ray films of the thoracic spine were normal.

A clinical diagnosis of eosinophilic meningitis due to *A cantonensis* was made. She was treated with bed rest, analgesia, antiemetics, and carbamazepine for her severe prominent hyperesthesia. A mild bilateral papilledema and a partial left third nerve palsy developed that resolved subsequently. She required further lumbar punctures for the relief of headaches. She was discharged from hospital a month after admission and returned to Vanuatu, where she is currently well. Serologic tests on admission were positive for *A cantonensis*.

Patients 3 and 4

Patient 2 had two sons, aged 11 and 12, who were transferred to the Austin Hospital five days after their mother's admission. Both had partially embraced their mother's new diet. They had similar though milder symptoms and signs and recovered more quickly than their mother. The younger son, patient 3, had a CSF pressure of 23 cm of water with a glucose level of 2.5 mmol per liter and a protein value of 0.54 grams per liter. The CSF cell count was as follows: neutrophils, 80, lymphocytes, 440, and eosinophils, 200 × 10^6 per liter (28% of total CSF leukocyte count). The older son, patient 4, had a CSF pressure of 30 cm of water, with a CSF glucose level of 3.2 mmol per liter and protein content of 0.50 grams per liter. His CSF contained 180 × 10^6 per liter lymphocytes, 120 × 10^6 per liter eosinophils (40% of total), and 170 × 10^6 per liter erythrocytes.

An independent 8-year-old daughter who had not cooperated with the family's dietary change remained well. The patient's husband had mild symptoms but was reluctant to be investigated.

Discussion

Angiostrongylus cantonensis is a parasite found in Australia,[1] Hawaii,[2] Thailand,[3] Japan, China, Vietnam, Cambodia, Papua New Guinea, Indonesia, the Philippines, Taiwan, Vanuatu, and several smaller Pacific Islands.[2] In previously reported Australian cases, infection has been acquired only in the state of Queensland, and patient 1 represents the first reported case of *A cantonensis* infection acquired in the state of New South Wales.

Adults of the rat lungworm, *A cantonensis,* reside and lay their eggs in the pulmonary arteries of rats and other rodents.[2] After hatching, the larvae break into the alveoli, migrate up the respiratory tract, are swallowed, and pass out with the feces. They develop into second- and third-

TABLE 1.—*Clinical Features of Patients With* Angiostrongylus cantonensis *Eosinophilic Meningitis*

Patient	Sex	Age, yr	Clinical Features	CSF Opening Pressure, cm water	CSF Protein, grams/liter	CSF Glucose, mmol/liter	Leukocyte Count (Eosinophil)* CSF, × 10^6/liter	Leukocyte Count (Eosinophil)* Blood, × 10^6/liter
1.....	M	25	Meningoencephalitis; residual neurologic sequelae; possible pulmonary and hepatic involvement	33	1.01	1.9	339 (0.22)	21.2 (0.29)
2.....	F	33	Severe meningitis; hyperesthesia; cranial nerve palsy	44	0.37	2.7	220 (0.22)	12.2 (0.22)
3.....	M	11	Mild meningitis	23	0.54	2.5	720 (0.28)	10.0 (0.18)
4.....	M	12	Moderate meningitis; hyperesthesia	30	0.50	3.2	310 (0.39)	8.4 (0.34)

CSF = cerebrospinal fluid

*Given as a fraction of 1.00.

stage larvae within their natural intermediate hosts, such as slugs and snails, notably the *Pila* species commonly eaten in Thailand. Freshwater prawns, land crabs, and frogs have been found to harbor the third-stage larvae of the parasite as a result of eating infected intermediate hosts. Humans, like rodents, become parasitized when they ingest infected molluscs, contaminated vegetables, or fomites. Larvae migrate to the brain, where they grow and subsequently travel to the lungs to deposit eggs. In humans, the nematode does not complete its life cycle, usually dying after reaching the central nervous system.[3]

A cantonensis infections are usually mild, with headache, nausea, photophobia, and neck stiffness as the predominant symptoms.[2] Severe peripheral paresthesia may be a diagnostic clue. Generalized weakness, visual disturbances, and extraocular muscle palsies are also well described,[2,3] but urinary retention, ataxia, and spinal cord lesions in humans are rare. Fever exceeding 38°C is uncommon.[5] Hepatic and pulmonary involvement have not been previously reported. Although not proved in the first case, no other cause was found for the pneumothorax and bronchopleural fistula or for the abnormal values on liver function tests. Resolution of the abnormal liver function correlated with the clinical resolution of the illness and with the administration of steroids.

Most cases of angiostrongyliasis in humans are self-limited, and recovery without sequelae is the rule. A number of cases of greater severity and chronicity have been reported, however, and these may correlate with a higher parasite load.[1,6] In patients 2, 3, and 4, the severity of the illness was directly related to the amount of unwashed lettuce each patient consumed.

The diagnosis of *A cantonensis* meningitis is suggested by the triad of typical clinical presentation, a history of exposure through eating intermediate hosts (such as shellfish) or contaminated food (such as unwashed watercress or lettuce), with cerebrospinal fluid eosinophilia. Staining of CSF for eosinophilia must usually be specifically requested. Positive serologic testing using an enzyme-linked immunosorbent assay is confirmatory.[7]

The differential diagnosis of *A cantonensis* meningitis includes cerebral cysticercosis, the only other infection in the Pacific region documented to occasionally cause CSF eosinophilia in excess of 10%.[8] Cerebral involvement with this parasite is rare and will usually present with symptoms or signs of a space-occupying lesion. In Southeast Asia, particularly Thailand, an intense eosinophilic pleocytosis can also be caused by *Gnathostoma spinigerum*.[3] The presenting symptom is often sharp pain from irritation of a nerve root. Myeloencephalitis with limb paralysis is common, and severe disabling sequelae may occur. The CSF is often bloody or xanthochromic. A serologic test for *Angiostrongylus* species does not cross-react with that for *G spinigerum*. *G spinigerum* is not known to occur in Australia or the Pacific Islands.

There have been a few reports of CSF eosinophilia associated with *Toxocara canis, Trichinella spiralis, Ascaris lumbricoides, Echinococcus granulosus,* and *Strongyloides stercoralis* infections.[8] In these cases, CSF eosinophilia is usually less than 10% and may be purely a result of intense peripheral eosinophilia. Similarly, neurosyphilis, tuberculous meningitis, and lymphomas may uncommonly cause mild CSF eosinophilia, but not to the degree seen in our patients.[8]

The optimal regimen for treatment is not established. Anecdotal reports exist for the efficacy of thiabendazole[3,9] and diethylcarbamazine citrate,[10] but anthelmintic drugs have not been shown conclusively to be beneficial in humans. Corticosteroids may be helpful in alleviating symptoms of raised intracranial pressure and in reducing allergic reactions to living or dead larvae.[2]

The disease is largely prevented through the control of rats. The proper washing of vegetables and cooking of snails and aquatic crustaceans are also important.

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Accidental Poisoning by Warfarin-Contaminated Herbal Tea

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AMERICAN CITIZENS, especially those living near the United States-Mexico border, frequently shop in Mexico. We report the case of a patient presenting with a coagu-

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